

By fax and mail:
00 41 22 733 5428

NEDERLANDSCH
OCTROOIBUREAU
EUROPEAN PATENT & TRADEMARK ATTORNEYS

10/510119

DT04 Rec'd PCT/PTO 04 OCT 2004

W.I.P.O.
P.O. Box 18
CH 1211 Geneva 20
Switzerland

Your ref.
Our ref. P207556PCT BSW/ja

The Hague, 2 September 2004

Re: International Patent Application No. PCT/NL03/00254
Applicant: Leiden University Medical Center

Dear Madam, Sir,

With reference to Rule 92bis.1(a)(ii), the applicant herewith request deletion of Robert S. Mittler as an inventor and for the US inventor/applicant form the above-identified International Application.

The reason for this deletion is that Mr. Mittler contributions as inventor relate solely to those aspects of the invention that concern the 4-1BB molecule and the therapeutic use of agonists of this molecule. However, during preliminary examination the applicant has amended the claims to overcome novelty and inventive step objections based inter alia on D1 (Melief et al., 2000, Adv. Immunol. 75: 235-282.) and based on the disclosures concerning the use of agonists of the 4-1BB molecule for anti-tumor therapy in D3 (Melero et al 1997, Nature Med 3, 682). As a result of these amendments, the present claims on which the IPER is based, no longer relate to the agonists of the 4-1BB molecule but instead relate exclusively to the anti-CD40 mono-therapy aspect of the application, which is inter alia based on the experiments in Example 12 of the application.

Since Mr Mittler did not contribute to these experiments or in any other way to this aspect of the invention his mention as an inventor would no longer be appropriate. The applicant therefore requests his deletion as an inventor and inventor/applicant from the above-identified International Application.

The representative,

Bar Swinkels

Correspondence: P.O. Box 29720 | 2502 LS The Hague | The Netherlands | E-mail: info@octrooibureau.nl

Bureau Den Haag: J.W. Frisolaan 13 | 2517 JS The Hague | T +31(0)70 331 25 00 | F +31(0)70 352 75 28 | Bureau Ede: Bennekomseweg 43 | 6717 LL Ede | T +31(0)318 707 000 | F +31(0)318 707 007

N.V. Nederlandsch Octrooibureau is ingeschreven bij de KvK Den Haag onder nr. 27263335 | De Algemene Voorwaarden vindt u op onze website

N.V. Nederlandsch Octrooibureau is registered with the Chamber of Commerce under no. 27263335 | The General Terms and Conditions can be found on our website

ABN AMRO NL54ABNA0430058594 Bic ABNANL2A | Rabo NL92RAB00129946001 Bic RABONL2U | ABN AMRO \$-account NL18ABNA0451715268 Bic ABNANL2A | BTW/VAT NL002605314801

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:

ATTORNEY'S DOCKET NUMBER

Linda DIEHL,
 Geertje VAN MIERLO,
 Cornelis J. M. MELIEF,
 Rene TOES
 and Rienk OFFRINGA

0470-045183

PCT/NL03/00254

ENTITLED

**"INDUCTION OF ANTI-TUMOR CTL IMMUNITY THROUGH
 IN VIVO TRIGGERING OF 4-1BB AND/OR CD40"**

To MAIL STOP PCT
 Attention: DO/EO/US
 Commissioner for Patents
 P.O. Box 1450
 Alexandria, VA 22313-1450

EXPRESS MAIL CERTIFICATE

"Express Mail" Label Number EV534966873US

Date of Deposit October 4, 2004

I hereby certify that the following attached papers or fees

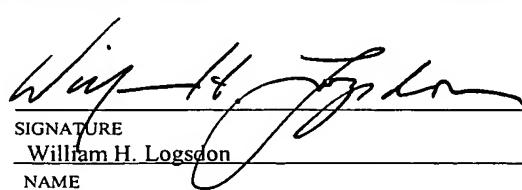
**TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/
 ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER
 35 U.S.C. 371 (original and two (2) copies) and check in amount
 of \$990.00 for filing fee and assignment recording fee
 DECLARATION AND POWER OF ATTORNEY (4 pp.)
 PRELIMINARY AMENDMENT with ABSTRACT
 WO 03/084999 – FRONT PAGE with ABSTRACT, SPECIFICATION,
 CLAIMS, DRAWINGS and SEARCH REPORT (63 pp.)
 LETTER to WIPO withdrawing ROBERT S. MITTLER as an inventor (1 p.)
 RECORDATION FORM COVER SHEET (1 p.) with ASSIGNMENT (3 pp.)**

are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. §1.10 on the date indicated above and is addressed to Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA, 22313-1450.

Nora Ann Pastrick
 (Typed name of person mailing paper or fee)

Nora Ann Pastrick
 (Signature of person mailing paper or fee)

Form PTO-1390 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE (REV 10-95) TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		ATTORNEY'S DOCKET NUMBER 470-045183
		U.S. APPLICATION NO. (If known) 107510119
INTERNATIONAL APPLICATION NO. PCT/NL03/00254	INTERNATIONAL FILING DATE 04.04.03 (April 4, 2003)	PRIORITY DATES CLAIMED 04.04.02 (April 4, 2002)
<p>TITLE OF INVENTION Assignee: LEIDEN UNIVERSITY MEDICAL CENTER</p> <p style="text-align: center;">INDUCTION OF ANTI-TUMOR CTL IMMUNITY THROUGH IN VIVO TRIGGERING OF 4-1BB AND/OR CD40</p>		
<p>APPLICANT(S) FOR DO/EO/US Linda DIEHL, Geertje VAN MIERLO, Cornelis J.M. MELIEF, Rene TOES and Rienk OFFRINGA</p>		
<p>Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items And other information:</p>		
<p>1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.</p> <p>2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.</p> <p>3. <input checked="" type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).</p> <p>4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.</p> <p>5. A copy of the International Application as filed (35 U.S.C. 371(c)(2))</p> <ol style="list-style-type: none"> <input type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau). <input checked="" type="checkbox"/> has been transmitted by the International Bureau. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). <p>6. <input type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)).</p> <p>7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))</p> <ol style="list-style-type: none"> <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau). <input type="checkbox"/> have been transmitted by the International Bureau. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. <input checked="" type="checkbox"/> have not been made and will not be made. <p>8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</p> <p>10. <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</p> <p>Items 11. to 16. Below concern document(s) or information included:</p> <p>11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</p> <p>12. <input checked="" type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</p> <p>13. <input checked="" type="checkbox"/> A FIRST preliminary amendment.</p> <p><input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment.</p> <p>14. <input type="checkbox"/> A substitute specification.</p> <p>15. <input type="checkbox"/> A change of power of attorney and/or address letter.</p> <p>16. <input checked="" type="checkbox"/> Other items or information:</p> <ol style="list-style-type: none"> WO 03/084999 Front Page with Abstract, Specification, Claims, Drawings and Search Report (63 pp.) Letter to WIPO withdrawing Robert S. Mittler as an inventor 		

U.S. APPLICATION NO. (If known) (37 CFR 1.5)	INTERNATIONAL APPLICATION NO. PCT/NL03/00254	ATTORNEY'S DOCKET NUMBER 470-045183	
17. <input checked="" type="checkbox"/> The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)): Search Report has been prepared by the EPO or JPO..... International preliminary examination fee paid to USPTO (37 CFR 1.482) No international preliminary examination fee paid to USPTO (37 CFR 1.482) But international search fee paid to USPTO (37 CFR 1.445(a)(2))..... Neither international preliminary examination fee (37 CFR 1.482) nor International search fee (37 CFR 1.445(a)(2)) paid to USPTO..... International preliminary examination fee paid to USPTO (37 CFR 1.482) And all claims satisfied provisions of PCT Article 33(2)-(4).....		CALCULATIONS PTO USE ONLY	
		\$950.00 \$750.00 \$790.00 \$1110.00 \$100.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =		\$ 950.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).		\$ 0.00	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE
Total claims	14 - 20 =	0	X \$18.00 \$ 0.00
Independent claims	1 - 3 =	0	X \$86.00 \$ 0.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)		+ \$290.00	\$ 0.00
TOTAL OF ABOVE CALCULATIONS =		\$ 950.00	
Reduction of 1/2 for filing by small entity, if applicable.		\$ 950.00	
SUBTOTAL =		\$ 950.00	
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +		\$ 0.00	
TOTAL NATIONAL FEE =		\$ 950.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property +		\$ 40.00	
TOTAL FEES ENCLOSED =		\$ 990.00	
		Amount to be: Refunded \$	
		Charged \$	
<p>a. <input checked="" type="checkbox"/> A check in the amount of <u>\$ 990.00</u> to cover the above fees is enclosed.</p> <p>b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.</p> <p>c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>23-0650</u>. A duplicate copy of this sheet is enclosed.</p>			
<p>NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.</p>			
SEND ALL CORRESPONDENCE TO: William H. Logsdon 700 Koppers Building 436 Seventh Avenue Pittsburgh, Pennsylvania 15219-1818 Telephone: (412) 471-8815 Facsimile: (412) 471-4094			
 <p>SIGNATURE William H. Logsdon</p> <p>NAME 22,132</p> <p>REGISTRATION NUMBER</p>			